

IN THE SPECIFICATION

Please amend the specification as follows:

On page 23, please replace the first paragraph with the following paragraph.

In all the constructions or compounds described herein, the antiangiogenic protein may be functionally attached to a specific leader peptide which can specify for secretion of the protein. For example and as described in the Example below, the antiangiogenic protein can have a signal sequence, such as an adenoviral signal sequence. An example is the adenovirus E19 signal sequence that can result in secretion of the antiangiogenic protein from the cell which is expressing the sequence encoding the antiangiogenic protein. A specific example of an adenovirus E19 signal sequence comprises the amino acid sequence MRYMILGLLALAAVCSAA (SEQ ID NO: 7). Other examples of signal sequences that can be used to facilitate secretion of an antiangiogenic protein include, but are not limited to, the murine Ig-kappa signal sequence (*Blezinger et al.* Nat. Biotechnol. 17: 343-8, 1999), rat insulin leader sequence (*Fakhral et al.* J. Immunother. 20: 437-8, 1997), FGF-4 signal sequence (*Ueno et al.* Atheroscler. Thromb. Vasc. Biol., 17: 2453-2460, 1997), human growth hormone signal peptide (*Rade et al.* Gene Ther. 6: 385-92, 1999), beta lactamase signal sequence (*Hughes et al.* Hum. Gene Ther. 5: 1445-55, 1994), bovine prolactin signal sequence (*Gorman et al.* Brain Res. Mol. Brain Res. 44:143-146, 1997) and other similar signal sequences. A functional attachment is typically, but not limited to, a peptide bond. Other additional sequences may also be attached to the antiangiogenic protein, either through the addition of a nucleic acid encoding the additional sequence, or by addition of a peptide to the antiangiogenic protein. Similarly, the specific antiangiogenic proteins of the present invention may be obtained not only through expression of a nucleic acid, but through the synthesis of a polypeptide as well. One skilled in the art will recognize that different nucleic acid sequences can encode the same polypeptide and therefore the exact sequence of the nucleic acid encoding the signal sequence can vary.

On page 40, please replace the second full paragraph with the following paragraph:

Cloning of murine endostatin. Murine endostatin was cloned by isolating RNA from the livers of 3 week old mice and converting the RNA to cDNA using a reverse transcriptase reaction.

Forward (gatctctagaccaccatgcatactcatcaggactttcag) (SEQ ID NO: 1) and reverse (gatcatcgatctatttgagaaagaggtca) (SEQ ID NO: 2) primers were used with this cDNA template to clone the murine endostatin cDNA into a sequencing plasmid (pkmendo-2). The PCR was performed using pfu enzyme with glycerol and DMSO as additives. The PCR conditions were: 94° C 45 sec, 50° C 45 sec, 25 cycles 70° C 2 min.

The sequence was confirmed using an automated sequencer.

On page 40, please replace the third full paragraph with the following paragraph:

Cloning of human endostatin. Human endostatin was cloned by isolating RNA from a human hemangioendothelioma. This RNA was converted to cDNA using a reverse transcriptase reaction and used as a template for PCR with the same conditions described above. The forward primer was gatctctagaccaccatggttgctcaacagccccctgt (SEQ ID NO: 3). The reverse primer was gatcatcgatctacttggaggcagtcataagct (SEQ ID NO: 4). The PCR product was cloned into a sequencing plasmid (pkhendo-2) and the sequence was confirmed using an automated sequencer.

On page 41, please replace lines 3-5 with the following:

Murine primer:

gatctctagaccaccatgaggtacatgatttaggcttgctcgccctgcggcagtcgcagcgcgcccatcactcatcaggactttcag (SEQ ID NO: 5)

On page 41, please replace lines 7-9 with the following:

Human Primer:

gatctctagaccaccatgaggtacatgatttaggcttgctcgccctgcggcagtcctccagcgcgccggtgcgctcaacagccccctg (SEQ ID NO: 6)

On page 44, please replace the first paragraph with the following paragraph:

Cloning of the murine endostatin gene. Murine cDNA was obtained by isolating RNA (RNeasy Mini Kit, Qiagen, Valencia, CA) from snap-frozen 2-week-old C57BL/6 mouse

(Charles River Laboratories, Wilmington, MA) liver and treating with Moloney murine leukemia virus reverse transcriptase (Life Technologies, Gaithersburg, MD). The murine endostatin gene was cloned into the TA cloning vector (Invitrogen, Carlsbad, CA) by polymerase chain reaction (PCR) using the primers *sense*: GATCTCTAGACCACCATGCATACTCATCAGGACTT (SEQ ID NO: 8) and *antisense*: ACTGGAGAAAGAGGTTTATCTAGCTACTAG (SEQ ID NO: 9). The 18-amino acid E3/19K signal sequence (MRYMILGLLALAAVCSAA) (SEQ ID NO: 7) was inserted upstream from the endostatin sequence by PCR using the primers *sense*: GATCTCTAGACCACCATGAGGTACATGATTTTAGGCTTGCTCGCCCTTGCGGC AGTCTGCAGCGCGGCCCATACTCATACTCATCAGGACTTTCAG (SEQ ID NO: 10) and *antisense*: as above. Plasmid DNA was amplified in DH5a cells (Life Technologies) and the signal sequence-murine endostatin (ss-mEndo) sequence was confirmed (ABI Prism 310 autosequencer, PE Applied Biosystems, Foster City, CA).